

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

to:

Commissioner  
 US Department of Commerce  
 United States Patent and Trademark  
 Office, PCT  
 2011 South Clark Place Room  
 CP2/5C24  
 Arlington, VA 22202  
 ETATS-UNIS D'AMERIQUE  
 in its capacity as elected Office

<b>Date of mailing</b> (day/month/year) 17 May 2001 (17.05.01)	
<b>International application No.</b> PCT/US00/21394	<b>Applicant's or agent's file reference</b> P50973
<b>International filing date</b> (day/month/year) 04 August 2000 (04.08.00)	<b>Priority date</b> (day/month/year) 06 August 1999 (06.08.99)
<b>Applicant</b> DIEDERICH, Ann, M. et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:  
14 February 2001 (14.02.01)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO  
 34, chemin des Colombettes  
 1211 Geneva 20, Switzerland

Authorized official

R. Forax

Facsimile No.: (41-22) 740 74 35

Telephone No.: (41-22) 338 33 39

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
15 February 2001 (15.02.2001)

PCT

(10) International Publication Number  
**WO 01/10822 A1**

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69/76, 235/00, 41/00, C07D 303/38

(21) International Application Number: PCT/US00/21394

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(25) Filing Language: English

(26) Publication Language: English

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60/147,576 6 August 1999 (06.08.1999) US

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(US).

(72) Inventors; and

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Beecham Corporation, Corporate Intellectual Property,  
UW2220, 709 Swedeland Road, P.O. Box 1539, King of  
Prussia, PA 19406-0939 (US).

(81) Designated States (national): AE, AL, AU, BA, BB, BG,  
BR, CA, CN, CZ, DZ, EE, GE, GH, GM, HR, HU, ID, IL,  
IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK,  
MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, TZ,  
UA, US, UZ, VN, YU, ZA.

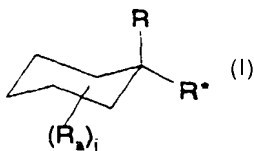
(84) Designated States (regional): ARIPO patent (GH, GM,  
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian  
patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European  
patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE,  
IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG,  
CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

**Published:**

— With international search report.

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: PROCESS FOR PREPARING ACIDS VIA ALPHA-CHLOROEOXY ESTERS



(57) Abstract: This invention relates to a method for preparing certain acids of formula (I) via a chloroepoxy ester, which are useful as phosphodiesterase 4 inhibitors.

WO 01/10822 A1

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/21394

**A. CLASSIFICATION OF SUBJECT MATTER**IPC(7) : C07C 255/00, 69/76, 235/00, 41/00; C07D 303/38  
US CL : 558/426; 560/059; 549/549; 564/171; 568/631, 644, 645

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**Minimum documentation searched (classification system followed by classification symbols)  
U.S. : 558/426; 560/059; 549/549; 564/171; 568/631, 644, 645

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
CAS on line, EAST. search terms used: cyclohexanoic acid, haloeipoxy ester and inhibitor.**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98/34584 A2 (SMITHKLINE BEECHAM CORPORATION) 13 August 1998	1-3 and 8-11, 13-19
A	US 5,552,438 A (CHRISTENSEN, IV) 03 September 1996 (03/09/96) see examples and	1-3 and 8-11, 13-16
A	US 5,602,173 A (CHRISTENSEN, IV) 11 February 1997 (11/02/97) see examples and	1-3 and 8-11, 13-16
A	US 5,605,923 A (CHRISTENSEN, IV et al.) 25 February 1997 (25/02/97) see examples	1-3 and 8-11, 13-16
A	claims. US 5,449,687 A (CHRISTENSEN, IV et al.) 12 September 1995 (12/09/95) see examples	1-3 and 8-11, 13-16
	claims.	

☐ Further documents are listed in the continuation of Box C.☐ See patent family annex.

\* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"Z" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

05 October 2000

Date of mailing of the international search report

20 NOV 2000

Name and mailing address of the ISA/US

Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Facsimile No. (703)305-3230

Authorized officer

Devsh Khare

Telephone No. (703) 308-1235

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/21394

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claim Nos.: 4-7  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:  
Claims 4 and 5 are not found. Claims 6 and 7 depend from claims 4 and 5.
3. ☒ Claim Nos.: 7 and 12  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐  
☐

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

## PATENT COOPERATION TREATY

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## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

REC'D 26 OCT 2001

WIPO

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Applicant's or agent's file reference <b>P50973</b>		<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. <b>PCT/US00/21394</b>	International filing date (day/month/year) <b>04 August 2000 (04.08.2000)</b>	Priority date (day/month/year) <b>06 August 1999 (06.08.1999)</b>	
International Patent Classification (IPC) or national classification and IPC <b>IPC(7): C07C 255/00, 69/76, 235/00, 41/00; C07D 303/380 and US Cl.: 558/426; 560/059; 549/549; 564/171; 568/631, 644, 645</b>			
Applicant <b>SMITHKLINE BEECHAM CORPORATION</b>			
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>4</u> sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of <u>   </u> sheets.</p> <p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the report</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input checked="" type="checkbox"/> Non-establishment of report with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p>			
Date of submission of the demand <b>14 February 2001 (14.02.2001)</b>		Date of completion of this report <b>25 September 2001 (25.09.2001)</b>	
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230		Authorized officer <i>Jaya Bridges</i> Devash Khare Telephone No. 703-308-0196	

Form PCT/IPEA.409 (cover sheet)(July 1998)

**I. Basis of the report**1. With regard to the **elements** of the international application: \*

- ☒ the international application as originally filed.
- ☒ the description:  
pages 1-13 \_\_\_\_\_ as originally filed  
pages NONE \_\_\_\_\_, filed with the demand  
pages NONE \_\_\_\_\_, filed with the letter of \_\_\_\_\_.
- ☒ the claims:  
pages 14-22 \_\_\_\_\_, as originally filed  
pages NONE \_\_\_\_\_, as amended (together with any statement) under Article 19  
pages NONE \_\_\_\_\_, filed with the demand  
pages NONE \_\_\_\_\_, filed with the letter of \_\_\_\_\_.
- ☐ the drawings:  
pages NONE \_\_\_\_\_, as originally filed  
pages NONE \_\_\_\_\_, filed with the demand  
pages NONE \_\_\_\_\_, filed with the letter of \_\_\_\_\_.
- ☐ the sequence listing part of the description:  
pages NONE \_\_\_\_\_, as originally filed  
pages NONE \_\_\_\_\_, filed with the demand  
pages NONE \_\_\_\_\_, filed with the letter of \_\_\_\_\_.

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of

- ☐ the description, pages NONE
- ☐ the claims, Nos. NONE
- ☐ the drawings, sheets/fig NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)). \*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\* Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/21394

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The question whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application,

☒ claims Nos. 4 -7 and 12

because:

☐ the said international application, or the said claim Nos. \_\_\_\_\_ relate to the following subject matter which does not require international preliminary examination (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. \_\_\_\_\_ are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. \_\_\_\_\_ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 4 -7, 12

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

# WRITTEN OPINION

International application No.  
PCT/US00/21394

## V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

### 1. STATEMENT

Novelty (N)	Claims <u>1-3, 8-11 and 13-19</u>	YES
	Claims <u>NONE</u>	NO
Inventive Step (IS)	Claims <u>NONE</u>	YES
	Claims <u>1-3, 8-11 and 13-19</u>	NO
Industrial Applicability (IA)	Claims <u>1-3, 8-11 and 13-19</u>	YES
	Claims <u>NONE</u>	NO

### 2. CITATIONS AND EXPLANATIONS

Claims 1-3, 8-11 and 13-19 lack novelty under PCT Article 33(2) as being anticipated by SMITHKLINE BEECHAM CORPORATION (WO 98/34584).

The claims are directed toward a process for preparing substituted cyclohexanoic acids, a process for making the intermediate compound (an epoxide cyclohexanoic formula) and the compounds (Claim 17-19).

SMITHKLINE BEECHAM CORPORATION discloses a method for preparing substituted cyclohexanoic acids by treating a compound of formula II (an epoxide cyclohexanoic formula) with lithium bromide or magnesium bromide in a polar solvent on pages 2-5 and in claims 1 and 2 and a process for making the intermediate (an epoxide cyclohexanoic acid formula) (see examples). The compounds are disclosed in claims 3 and 4. The processes and compounds claims of the present invention are anticipated by the reference.

----- NEW CITATIONS -----



# PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

To:  
JAMES M. KANAGY  
SMITHKLINE BEECHAM CORPORATION  
CORPORATE INTELLECTUAL PROPERTY, UW2220  
709 SWEDELAND ROAD, P.O. BOX 1539  
KING OF PRUSSIA, PA 19406-0939

## PCT

### NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

Applicant's or agent's file reference P50973	Date of Mailing (day/month/year) <span style="font-size: 1.2em;">20 NOV 2000</span>
International application No. PCT/US00/21394	International filing date (day/month/year) 04 August 2000 (04.08.2000)
Applicant SMITHKLINE BEECHAM CORPORATION	

1. ☒ The applicant is hereby notified that the international search report has been established and is transmitted herewith.  
**Filing of amendments and statement under Article 19:**  
 The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

**When?** The time limit for filing such amendments is normally 2 months from the date of transmittal of the international search report; however, for more details, see the notes on the accompanying sheet.

**Where?** Directly to the International Bureau of WIPO  
 34, chemin des Colombettes  
 1211 Geneva 20, Switzerland  
 Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after 18 months from the priority date, the international application will be published by the International Bureau.  
 If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in rules 90 bis 1 and 90 bis 3, respectively, before the completion of the technical preparations for international publication.

Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230	Authorized officer <div style="text-align: center;">                       Jayel Bridges                      Devesh Khare                 </div> Telephone No. (703) 308-1235
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